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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,072	07/30/2003	Frank Paul	P32168	9432
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GLAXOSMITHKLINE Corporate Intellectual Property - UW2220 P.O. Box 1539 King of Prussia, PA 19406-0939			EXAMINER LARKIN, DANIEL SEAN	
			ART UNIT 2856	PAPER NUMBER

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

K1

<b>Office Action Summary</b>	<b>Application No.</b> 10/630,072	<b>Applicant(s)</b> PAUL ET AL.	
	<b>Examiner</b> Daniel S. Larkin	<b>Art Unit</b> 2856	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 July 2003.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-10 and 12-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 12-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/830,396.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Priority***

1. Acknowledgment is made of Applicants' claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/830,396, filed on 29 June 2001.

### ***Specification***

2. The abstract of the disclosure is objected to because of the following:  
  
Abstract line 6: A -- comma -- should be inserted after the term "Preferably".  
  
Abstract lines 9-11: The sentence "It is desirable that the drive signal..." is inappropriate because the abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art. Correction is required. See MPEP § 608.01(b).
3. The disclosure is objected to because of the following informalities:  
  
Page 1, line 2: The phrase --, now U.S. Patent No. 6,647,764 -- should be inserted after the date "21 October 1999".  
  
Page 1, line 14: A -- comma -- should be inserted after the term "Typically".  
  
Page 1, line 17: A -- comma -- should be inserted after the term "materials".  
  
Page 1, line 18: A -- comma -- should be inserted after the abbreviation "KDP" and the term "salt".  
  
Page 1, line 23: A -- comma -- should be inserted after the term "silver".  
  
Page 1, line 31: A -- comma -- should be inserted prior to the term "but".

Page 2, line 2: A -- comma -- should be inserted after the term "Thus".

Page 2, line 13: A -- comma -- should be inserted after the term "Typically".

Page 2, line 28: A -- comma -- should be inserted after the term "liquid".

Page 3, line 1: A -- comma -- should be inserted after the term "sensitivity".

Page 3, line 10: A -- comma -- should be inserted after the term "Typically".

Page 3, line 24: A -- comma -- should be inserted prior to the term "but".

Page 4, line 1: A -- comma -- should be inserted after the term "embodiment".

Page 4, line 2: A -- comma -- should be inserted after the term "Preferably".

Page 5, line 8: The conjunction -- and -- should be inserted after the term "circuit".

Page 5, line 17: A -- comma -- should be inserted after the term "typically".

Page 5, line 19: A -- comma -- should be inserted after the numeral "3".

Page 5, line 28: A -- comma -- should be inserted after the term "Alternatively".

Page 5, line 31: A -- comma -- should be inserted after the term "Thus".

Page 5, line 32: The "colon" after the term "resistor" should be corrected with a -- semicolon --; and a -- comma -- should also be inserted after the term "alternatively".

Page 6, line 3: A -- comma -- should be inserted after the term "However".

Page 6, line 21: A -- comma -- should be inserted after the first occurrence of the term "liquid".

Page 6, line 29: A -- comma -- should be inserted after the term "below".

Page 7, line 15: A -- comma -- should be inserted after the numeral "3".

Page 8, line 9: Reference numeral "52" should be corrected to read -- 62 --.

Page 8, line 15: A -- comma -- should be inserted after the term "such".

Page 8, line 21: A -- comma -- should be inserted after the numeral "4a".

Page 8, line 26: A -- comma -- should be inserted after the term "input" and after the numeral "46A".

Page 8, line 27: A -- semicolon -- should be inserted after the term "above"; and a -- comma -- should be inserted after the term "but".

Page 8, line 30: A -- comma -- should be inserted after the term "embodiment".

Page 8, line 31: A -- comma -- should be inserted after the numeral "46C".

Page 9, line 6: A -- comma -- should be inserted after the numeral "56".

Page 9, line 11: A -- comma -- should be inserted after the terms "Thus" and "output".

Page 9, line 15: A -- comma -- should be inserted after the term "shown".

Page 9, line 31: A -- comma -- should be inserted after the numeral "6".

Page 9, line 32: The markings after the term "be" and example" should be corrected with -- commas --.

Page 10, lines 13 and 15: The term "O ring" should be corrected to read -- O-ring --.

Page 11, line 10: A -- comma -- should be inserted after the term "configuration".

Page 11, line 25: The numeral "20" should be corrected to read -- twenty --.

Appropriate correction is required.

***Claim Objections***

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4. Claims 4, 12, 16, and 19-27 are objected to because of the following informalities

Re claim 4, claim line 2: A -- comma -- should be inserted after the second occurrence of the term "means".

Re claim 12, claim line 1: One occurrence of the term "in" should be deleted.

Re claim 16, claim line 1: The term "antibody" has been misspelled.

Re claim 19, claim line 4: The article "an" should be replaced with the phrase -- a first -- since a second output signal is also recited in the claim.

Re claim 21, claim line 5: The term "it" should be replaced with the phrase -- drive signal --. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

5. Claims 7, 12-18, 20-27, and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention.

Re claim 7, claim line 1: The phrase "the feedback loop" lacks antecedent basis.

Re claim 12, claim lines 1 and 2: This claim does not make sense.

Re claim 13, claim line 1: The claim fails to further limit the apparatus recited in claim 1 since claim 13 provides method limitations for the apparatus. Moreover, the claim fails to recite the necessary steps for measuring the density of a liquid using the apparatus of claim 1.

Re claim 14, claim line 1: The claim fails to further limit the apparatus recited in claim 1 since claim 14 provides method limitations for the apparatus. Moreover, the

claim fails to recite the necessary steps for measuring the viscosity of a liquid using the apparatus of claim 1.

Re claim 15, claim lines 1 and 2: The claim fails to further limit the apparatus recited in claim 1 since claim 15 provides method limitations for the apparatus. Moreover, the claim fails to recite the necessary steps for detecting an interaction between a cell and a target material using the apparatus of claim 1.

Re claim 16, claim lines 1 and 2: The claim fails to further limit the apparatus recited in claim 1 since claim 16 provides method limitations for the apparatus. Moreover, the claim fails to recite the necessary steps for detecting a titre of antibody-antigen agglutination using the apparatus of claim 1.

Re claim 17, claim lines 1 and 2: The claim fails to further limit the apparatus recited in claim 1 since claim 17 provides method limitations for the apparatus. Moreover, the claim fails to recite the necessary steps for monitoring, in solution, a bacterial characteristic using the apparatus of claim 1.

Re claim 18, claim lines 1 and 2: The claim fails to further limit the apparatus recited in claim 1 since claim 18 provides method limitations for the apparatus. Moreover, the claim fails to recite the necessary steps for measuring the concentration of bacteria in a solution using the apparatus of claim 1.

Re claim 20, claim line 2: The phrase "the first output signal" lack antecedent basis.

Re claim 21, claim lines 1-6: The claim is deemed to be indefinite because the claim recites a method of "measuring a characteristic of an oscillating piezoelectric

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sensor"; however, the claim fails to actually recite a step of measuring a characteristic of an oscillating piezoelectric sensor. The claim only recites providing a drive signal to the sensor and controlling/maintaining the drive signal.

Re claim 27, claim lines 1 and 2: The claim fails to recite the necessary steps for detecting cells or biochemically active compounds using the method of claim 21.

Re claim 32, claim line 1: The claim fails to further limit the apparatus recited in claim 1 since claim 32 provides method limitations for the apparatus. Moreover, the claim fails to recite the necessary steps for conducting an immunoassay using the apparatus of claim 1.

### ***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

6. Claims 4, 5, and 8 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 7, and 8 of prior U.S. Patent No. 6,647,764. This is a double patenting rejection.



With respect to claim 4, this claim is substantially identical to claim 1 of the patent. Claim 1 of the patent is a combination of claims 1, 2, and 4 of the application.

With respect to claim 5, this claim is substantially identical to claim 7 of the patent. Claim 7 of the patent is a combination of claims 1 and 5 of the application.

With respect to claim 8, this claim is substantially identical to claim 8 of the patent. Claim 8 of the patent is a combination of claims 1, 2, and 8 of the application.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-3, 6, 7, and 9 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,647,764. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following:

With respect to claim 1, this claim is broader than the counterpart patent claim, claim 1; however, all of the limitations of application claim 1 are found within patented claim 1.

With respect to claim 2, this claim is broader than the counterpart patent claim, claim 1; however, all of the limitations of application claim 2 are found within patented claim 1.

With respect to claim 3, this claim is broader than the counterpart patent claim, claim 2; however, all of the limitations of application claim 3 are found within patented claim 2.

With respect to claim 6, this claim is broader than the counterpart patent claim, claim 3; however, all of the limitations of applications claim 6 are found within patented claim 3.

With respect to claim 7, this claim is broader than the counterpart patent claim, claim 4; however, all of the limitations of application claim 7 are found within patented claim 4.

With respect to claim 9, this claim is broader than the counterpart patent claim, claim 5; however, all of the limitations of application claim 9 are found within patented claim 5.

### ***Claim Rejections - 35 USC § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1-3, 6, 7, 9, 12, 21, 23, 25, 28, and 30-32 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US 4,788,466 (Paul et al.).

With respect to the limitations of claims 1 and 21, the reference to Paul et al. discloses a piezoelectric sensor (13) coupled to an oscillation circuit for driving the sensor to maintain its vibration despite changes in the fluid medium (col. 2, lines 27-31).

With respect to the limitation of claim 2, the oscillation circuit includes an amplifier (21) with feedback coupling to form a feedback loop and a second amplifier (17) which acts as a variable gain means.

With respect to the limitations of claim 3, the reference discloses a second/gain control output input to the amplifier (17) which is combined with a signal from the piezoelectric sensor to provide a gain control signal of the variable gain means.

With respect to the limitation of claim 6, the reference states that the piezoelectric sensor (13) produces a substantially sinusoidal output which allows one to presume that the drive signal is also sinusoidal.

With respect to the limitation of claim 7, the reference states that the amplifiers (17, 21) of the feedback loop are preferably linear as respects the amplifier signal, but

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may be either linear or non-linear in respect to the response to the gain control input signal (col. 7, lines 42-46).

With respect to the limitation of claim 9, the reference states that the piezoelectric sensor (13) is comprised of an AT cut quartz crystal.

With respect to the limitation of claim 23, the reference discloses that the changes in the frequency of the sensor are monitored and corrected to maintain a consistent vibration of the sensor.

With respect to the limitation of claim 25, the reference discloses that the fluid is liquid.

With respect to the limitation of claim 28, the reference to Paul et al. discloses a piezoelectric sensor (13) oscillated at a resonant frequency through an oscillation circuit. The oscillation circuit includes an amplifier (21) with feedback coupling to form a feedback loop and a second amplifier (17) which acts as a variable gain means to maintain a constant drive signal to the sensor.

With respect to the limitations of claim 30, the reference discloses a second/gain control output input to the amplifier (17) which is combined with a signal from the piezoelectric sensor to provide a gain control signal of the variable gain means.

With respect to the limitation of claim 31, the reference states that the amplifiers (17, 21) of the feedback loop are preferably linear as respects the amplifier signal, but may be either linear or non-linear in respect to the response to the gain control input signal (col. 7, lines 42-46).

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11. Claims 1, 2, 9, 10, 12, 15-18, 21, 23, 25, 27, 28, and 32 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over "A High Stability Quartz Crystal Microbalance Electrode for Simultaneous Solution-Phase Electrochemistry/Microgravitometry" (Komplin et al.).

With respect to the limitations of claims 1, 2, 21, and 28, the article to Komplin et al. discloses a quartz crystal microbalance oscillator circuit which incorporates a high-gain feedback amplifier controlled by an automatic gain network. Signal level in the oscillator feedback loop is automatically optimized to provide sufficient gain necessary to sustain stable oscillation (abstract).

With respect to the limitation of claim 9, the article recites that the sensor is an AT-cut quartz radio crystal.

With respect to the limitation of claims 10, 12, and 25, the article states that sensor is placed in a liquid sample cell for use in electrochemistry/microgravitometry experiments (see Figure 8). One of ordinary skill in the art would recognize that the liquid utilized may interact with a material of chemical or biological origin.

With respect to the limitation of claims 15-18, 27, and 32, the Examiner argues that one of ordinary skill in the art would recognize the many uses of the sensor given that the article recites that the quartz crystal microbalance can be coated with compounds which selectively absorb analytes of interest; the microbalance may be coated with a film to measure ppm concentrations of ammonia. Additional uses include applying the microbalance to solution phase sensing and electrochemical studies, Langmuir-Blodgett films, electrodeposition of conductive polymers and molecular

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metals, enzymatic studies, and immunoassay techniques (page 1520, left column, first paragraph).

With respect to the limitation of claim 23, the article states frequency counters are capable of discerning tiny frequency shifts although the authors prefer to monitor a voltage level which varies directly with mass change (page 1533, left column, first full paragraph).

12. Claims 19 and 20 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over "Quartz Crystal Microbalance Setup for Frequency and Q-Factor Measurements in Gaseous and Liquid Environments" (Rodahl et al.).

With respect to the limitations of claims 19 and 20, the article to Rodahl et al. discloses a quartz crystal microbalance constructed for simultaneous measurement of the frequency, the absolute Q factor, and the amplitude of oscillation of the crystal microbalance. The crystal is driven at the crystal's resonant frequency by an oscillator circuit.

13. Claims 1, 2, 9, 12-14, 21, 22, 24, 25, and 28 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over "An Electronic Oscillator With Automatic Gain Control: EQCM Applications" (Chagnard et al.).

With respect to the limitations of claims 1, 21, and 28, the article to Chagnard et al. discloses an oscillator for use with an acoustic wave sensor. The oscillator monitors the resonance frequency of the sensor and provides an automatic gain control signal that monitors the energy dissipated by the sensor (abstract). The article states that the purpose of the automatic gain circuit is to keep the motional amplitude of the crystal at a constant level.

With respect to the limitation of claim 9, the article states that the acoustic sensor is an AT-cut quartz crystal.

With respect to the limitation of claims 12 and 25, the article states that the sensor is in contact with liquid.

With respect to the limitation of claims 13 and 22, the article provides a formula which appears to allow one to solve for density of a liquid from voltage of the automatic gain control circuit and the bulk liquid viscosity (see Equation 9, page 133). The article also discloses that density and viscosity values can be estimated from previously determined calibration curves (page 134, right column, first full paragraph).

With respect to the limitation of claim 14, the article states that the sensor was used to determine viscosity values of different concentrations of an ethylene glycol, mixture (page 132, right column, first paragraph).

With respect to the limitation of claim 24, the article provides an equation for solving for the quality factor (Q) of the sensor/resonant system (see Equations 3 and 4, page 133, right column).

14. Claims 1, 2, 9, 12-14, 21-23, 25, 28, and 29 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US 4,783,987 (Hager et al.).

With respect to the limitations of claims 1 and 21, the reference to Hager et al. discloses an analysis system comprised of a piezoelectric crystal exposed to an energy-absorptive medium of interest. An oscillation circuit is included for sustaining oscillation of the crystal in contact with the fluid (abstract). Although, not expressly stated, the Examiner argues that oscillating the crystal at the crystal's resonant frequency is well within the purview of one of ordinary skill in the art.

With respect to the limitations of claims 2 and 28, the reference also discloses that the oscillator circuit includes feedback elements for providing automatic gain control of the amplifier portion of the oscillator (abstract).

With respect to the limitation of claim 9, the reference discloses that the piezoelectric crystal is an AT-cut quartz crystal (col. 6, lines 7-12).

With respect to the limitations of claims 12 and 25, the reference discloses that the sensor is placed into a liquid.

With respect to the limitations of claims 13, 14, 22, and 23, the reference discloses that the sensor may be used to detect fluid characteristics, such as viscosity and density (abstract). Additionally, the reference states if one fluid characteristic is allowed to vary, the characteristic can be measured by monitoring the frequency of oscillation of the piezoelectric element and comparing that frequency with empirically derived data correlating frequency and the characteristic of interest (col. 5, lines 5-12).



With respect to the limitation of claim 29, the reference states that the automatic gain control output of an operational amplifier (46) at a point (D) allows the loop gain of the circuit to be maintained at a level exactly equal to +1, independent of other changes (col. 13, lines 26-32).

15. Claims 1, 2, 6, 9, 12, 19-21, 24, 25, and 28 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over "Development of Circuit for Measuring Both Q Variation and Resonant Frequency Shift of Quartz Crystal Microbalance" (Nakamoto et al.).

With respect to the limitations of claims 1, 2, 6, 9, 19, 20, 21, 23, 24, and 28, the article to Nakamoto et al. discloses a quartz crystal microbalance comprising an oscillation circuit to apply a constant sinusoidal RF voltage to the microbalance through an automatic gain control amplifier (page 807, right column, Figure 3b). The article also states that quartz crystal microbalances are well known in their use as analysis apparatus (page 806, left column, first paragraph). The article discloses that a circuit has been developed to measure both Q variation and resonant frequency shift of a quartz crystal microbalance.

With respect to the limitations of claims 12 and 25, the article recites that the microbalance may be immersed in a liquid (page 810, right column, first paragraph).

16. Claims 10, 15-18, 26, 27, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,788,466 (Paul et al.) in view of EP 215669 (Karube et al.).

The reference to Paul et al. fails to expressly state that the material of chemical or biological origin is attached to the surface of the crystal; or using the crystal in different biosensor applications; or placing the sensor in a flowing liquid. The reference does recite that the sensor may be used to monitor electrochemical deposition, DNA Hybridization, corrosion studies, bio-chemical studies concerning enzyme analysis or water quality, or any situation where molecules are attracted to or leave from a surface surrounded by a liquid.

The reference to Karube et al. discloses an analytical device and method for analysis of biochemicals, microbes, and cells using a piezoelectric crystal biosensor. The reference discloses that a biochemical or organic compound is applied to the surface of the crystal. The crystal is then allowed to adsorb biochemicals, microbes, or cells of interest and the resonant frequency of the weighted crystal is determined and compared with a calibration curve obtained previously to determine the concentration of the biochemicals, microbes, or cells. The reference also states that the resonant frequency of the sensor varies according to the temperature, conductivity, and flow rate of the liquid, therefore measurements in an antigen-antibody reaction are carried out by replacing solutions with distilled water and feeding distilled water stored in a thermostatically controlled bath to a cell at a constant rate (page 4, lines 40-49). Utilizing the piezoelectric sensor as a biosensor would have been obvious to one of ordinary skill in the art given that changes in the resonant frequency of the sensor due to mass changes is easily determined which in turn is a direct function of the

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concentration of elements of interest. Providing a flowing liquid allows one to monitor changes in frequency of the crystal prior to elution or washing of the crystal.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel S. Larkin whose telephone number is 571-272-2198. The examiner can normally be reached on 8:00 AM - 5:00 PM Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Hezron Williams can be reached on 571-272-2208. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel Larkin  
AU 2856  
04 March 2004



**DANIEL S. LARKIN**  
**PRIMARY EXAMINER**